Incidence rates of oral cancer and oral pre-cancercous lesions in a 6-year follow-up study of a Taiwanese aboriginal community

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BACKGROUND: In a previous article, we reported the prevalence rates of oral mucosal lesions in an aboriginal community from an epidemiological survey of oral precancerous lesions.

METHODS: Since 1997, the authors have started regular follow-up of the study population originally investigated. Thus, it has been possible to obtain incidence rates for the various oral pre-cancerous lesions and conditions.

RESULTS: There were 194 persons without any oral lesion in the 1997 screening. During the clinical follow-up investigation and during the analysis of biopsies from pre-cancerous lesions, we discovered six new lesions (including cancer and pre-cancerous lesions) from five participants. All of the five persons were areca/betel quid chewers, and only one mixed areca/betel quid chewing with cigarette smoking habit. The age-standardized incidence rates for quid lesion, oral submucous fibrosis (OSF) and squamous cell carcinoma (SCC) were 267.0, 374.1 and 146.2 per 100 000 person-years, respectively, for areca/betel quid chewers.

CONCLUSIONS: As compared with the rates from India and the general Taiwanese population, the study community encountered a serious problem of oral lesions. J Oral Pathol Med (2005) 34: 596–601

Keywords: areca/betel quid; epidemiology; incidence; leukoplakia; oral submucous fibrosis

Introduction

Areca/betel quid related lesions have become a major public health concern in Taiwanese society. A recent survey showed that 8.5% of people aged 18 years or older were current areca/betel quid chewers (1). In 2003, oral cancer was named as the fifth highest cause of cancer death in Taiwan for men (the seventh for both men and women). Hence, it is crucial for the local health authority and public health workers to understand the prevalence as well as incidence rates of areca/betel quid related lesions.

The incidence rates for oral cancer are available for many countries, including Taiwan, with a national cancer registry system. However, in terms of prevention, knowing the incidence rate of cancer can be somewhat late for early detection. Hence, to understand the incidence rates of areca/betel related lesions will be very helpful to implement a plan for oral cancer prevention. Previous studies have shown little information about incidence rates of oral lesions, except in India. However, unlike most of the areca quid in India, tobacco is never added to the areca/betel quid of Taiwan. Hence, the incidence rates of lesions with areca/betel quid only and without tobacco remain unknown.

The authors initiated an epidemiological survey on oral mucosal lesions in March, 1997, and found that the prevalence of lesions was 34.1% (2). Since 1997, the authors have been able to maintain at least 1 day dental clinic per week in Mutan, an aboriginal community in Southern Taiwan, and many oral mucosal lesions were discovered and confirmed pathologically. The purpose of this study was to discuss the incidence rates of oral cancer and oral pre-cancerous lesions among the community with high prevalence rates of areca/betel quid chewing habit.

Materials and methods

Study population and sampling

The total population aged 20 years old and older in Mutan was 3623 (55.7% men and 44.3% women) according to the 1996 Official Household Registry. In 1997, the sample of 312 participants was based on a

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stratified random survey sampling study with six strata in different combination of gender (men and women) and age groups (20-39 years old, 40-59 years old, 60 and above years old). Within each stratum, a systematic sample of adults aged 20 years and above was identified. It was designed to recruit 501 persons into the sample, and 312 persons finished clinical examinations for oral lesions and interviews for their areca/betel guid chewing and cigarette smoking habit. Because of lacking job opportunities, most men or young people have to earn their livings from outside of their hometown, and keep their children and parents at home for saving expenses. Hence, it is typical in this society that each household has some family members moving out of town. During our study, most of the time we found that elderly, women and children are more likely to stay in hometown. Mutan, Ping-tong county, has a long history of areca/betel quid chewing habits.

Follow-up

Since the closure of the epidemiological survey (2) in 1997, in order to follow-up the necessary treatment of patients with pathologically confirmed lesions, and to continue screening for the rest of the residents in the community, a weekly dental clinic was first set-up in Mutan. Participants in a 1997 survey were monitored and followed-up. As shown in Table 1, among the 312 participants, there were 194 persons without any oral lesion during the 1997 screening. Given that 167 of these participants had lifetime chewing experiences, and 121 of them still has chewing habit in 1997, it was felt by the authors that these people were still at high risk of developing lesions. For the rest of the 312 original individuals examined (118 persons), 50 participants were successfully finished biopsies, and only one person developed another new lesion later. Some participants refused their biopsy taken.

Areca/betel quid

The ingredients of areca/betel quid usually vary with demography in Taiwan. The primary types of areca/betel quid in Mutan include: (i) the betel quid, which is made by wrapping an unripe areca fruit and slaked lime paste with a piece of betel leaf, and (ii) the stem quid, an areca quid, which is only seen in southern parts of aboriginal areas. The stem quid is made by putting a piece of stem of *Piper betle* Linn. with white lime paste (slaked lime) into an unripe areca fruit [see Figs 2 and 3 of Yang et al. (2)].

The fresh unripe areca fruit, an essential ingredient, is used in Taiwanese chewing quid instead of using ripe areca nut in the betel quid of other southeast Asian countries. Tobacco is never added in any types of the chewing quid.

Lesions

In 1997 survey, participants were examined by a dentist for oral mucosal lesions based on the criteria recipe described in Zain (3). One type of target oral mucosal condition (oral submucous fibrosis, OSF) and two types of target oral mucosal lesions (oral cancer and leukoplakia) were recorded. In this study, 194 participants free of the above lesions were followed-up. The incidences of hyperparakeratosis and epithelial hyperplasia were grouped as quid lesion in the following of this paper.

Statistical analysis

The age-standardized incidence rates were computed based on the age group population proportions of the World Standard Population (4). The confidence intervals for the incidence rates were computed based on Esteve et al. (5). According the chewing habits, the follow-up participants can be divided into three groups: group 1, 27 subjects with no chewing habit in lifetime; group 2, 46 subjects had chewing habit before but stopped before the 1997 survey; and group 3, 121 subjects had chewing habit in 1997. Essentially, all the new lesions occurred in the 121 participants with areca/ betel quid chewing habit in 1997. Those who did not have chewing habit in their lifetime or had stopped the habit before 1997 did not develop any lesions during 1997-2003. The age-standardized incidence rates were calculated based on the groups mentioned above.

Results

For those without any lesions seen in 1997, during the follow-up checks were first examined by dentists, and then biopsies were taken and confirmed histologically. There were five persons with six newly developed lesions found during 1998–2003: one squamous cell carcinoma (SCC), two OSF and three quid lesions (two hyperparakeratosis and one epithelial hyperplasia) (Table 2). All of the six lesions from five participants (one man and four women) detected during the follow-up surveys were in persons who had normal oral mucosa at the time of first examination. Their ages ranged from 47 to 78 years old (average 60.8). All of them had areca/betel quid chewing habit in 1997 with a chewing duration ranging from 37 to 49 years, and a daily chewing amount ranged from 20 to 55 guid a day. Three of the participants chewed betel quid, one chewed stem quid, and one chewed both the betel quid and stem quid. The four women had no prior history of cigarette smoking, while the man had quid chewing and cigarette smoking habit. Regardless of the cigarette smoking habits, no new lesions were found among the non-areca/betel quid chewers or those who had stopped the habit in 1997. All of the new lesions were on buccal sites.

The age-standardized incidence rates for all lesions (sum of OSF, quid lesions and SCC) and OSF are shown in Table 3, and those for quid lesions and SCC are in Table 4. In terms of the World Standard Population, OSF had the highest incidence rate of 195.8 per 100 000 person-years, and 374.1 for areca/betel quid chewers. Among the areca/betel quid chewers, the incidence of men (384.6 per 100 000 person-years) was higher than that of women (285.7 per 100 000 person-years).

The incidence rate of quid lesions (Table 4) was 122.2 per 100 000 person-years, and 267.0 for areca/betel quid chewers. In similar to OSF, men also had higher

Table 1 Population characteristic of Mutan county

		Percentage of		Numb	per of persons wi	th no oral lesion			
Age group (year)	Number in study sample	Current betel quid chewers in 1997	Having either OSF or leukoplakia in 1997	Toal	With lifetime chewing habit	With chewing habit in 1997	Developed new lesion during 1998–2003	Number of new lesions	Name of lesions
Men									
20-39	25	56.0	20.0	20	18	11	0	0	
40-59	45	66.7	31.1	31	26	18	0	0	
≥60	49	57.1	42.9	28	19	12	1	2	Quid lesion & OSF
Women									
20-39	38	73.7	13.2	33	29	23	0	0	
40–59	59	84.7	39.0	36	32	29	3	3	SCC, quid lesion, OSF
≥60	96	76.0	52.1	46	43	28	1	1	Quid lesion
Total	312			194	167	121	5	6	

Numbers of first three columns were cited from Table 1 of Yang et al. (2).

Table 2	Basic in	formation	of ne	wly	developed	lesion	between	1998	and	2003
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Sex	Age in 1997	Year of diagnosis	Lesion	Site	Areca/betel quid chewing	Years of chewing quid	Number of quid/day	Types of quid	Cigarette smoking	Years of smoking	Number of cigarettes/day
Female	47	2002	OSF	Buccal	Yes	37.6	20	Betel quid and stem quid	No		
Female	54	2000	SCC	Buccal	Yes	36.5	30	Betel quid	No		
Female	56	2001	Quid lesion	Buccal	Yes	36.6	55	Stem quid	No		
Female	78	2003	Quid lesion & mucositis	Buccal	Yes	48.8	30	Betel quid	No		
Male	69	1998	Quid lesion & OSF	Buccal	Yes	45.2	30	Betel quid	Yes	49	40
Average	60.8					40.9	33				

Table 3	Age adjusted in	cidence rate ((per 100	000 perso	n-year) of	new lesions
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		All lesions				OSF						
Group	Number of persons followed	Number of cases	Person-year	Incidence	95% CI (upper–lower)	Number of cases	Person-year	Incidence	95% CI (upper–lower)			
Total												
Men	79	1	475	161.3	-545.6-868.2	1	475	161.3	-545.6-868.2			
Women	115	4	685	534.5	-316.9-1385.9	1	689	212.8	-204.3-629.8			
Total	194	5	1154	211.6	-80.3-503.5	2	1158	195.8	-170.5 - 562.1			
Areca/betel	quid chewing hab	it										
Men	41	1	253	384.6	-1301.0-2070.3	1	253	384.6	-1301.0-2070.3			
Women	80	4	475	671.1	-366.8 - 1709.1	1	479	285.7	-274.3-845.7			
Total	121	5	716	375.6	-205.1-956.3	2	720	374.1	-446.7-1194.8			

Table 4	Age adjusted	incidence 1	rate (per	100 000	person-year)	of new	lesions
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		Quid lesion				SCC						
Group	Number of persons followed	Number of cases	Person-year	Incidence	95% CI (upper–lower)	Number of cases	Person-year	Incidence	95% CI (upper-lower)			
All popula	tion											
Men	79	1	475	161.3	-545.6 - 868.2	0	475	0.0	-			
Women	115	2	689	108.1	-49.3-265.5	1	687	213.7	-511.7-939.1			
Total	194	3	1158	122.2	-138.5-382.8	1	1161	89.6	-214.6-393.8			
Areca/bete	l quid chewing hat	bit										
Men	41	1	253	384.6	-1301.0-2070.3	0	126	0.0	_			
Women	80	2	479	132.9	-36.8 - 302.6	1	144	252.5	-604.8-1109.8			
Total	121	3	720	267.0	-451.6-985.6	1	276	146.2	-350.1-642.5			

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Table 5	Comparison	of incidence	rates (per	100 000	person-years)	of leukoplakia	in India	with the	current study
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		Male			Female			Total		
Area (years of follow-up)	Habits	Person-years	New cases	Incidence per 100 000 person-year	Person-years	New cases	Incidence per 100 000 person-year	Number of persons	% of new cases	
Gujarat (11) (2 years in 57 518 factory workers) Mumbai (13) (10 years in	Betel quid Betel quid and smoke Tobacco quid Tobacco quid and smoke							80 585 130	3.8% 6.2% 11.2% 8.9%	
3674 policemen)										
Ernakulam (12)	No habit	5792	-	-	24 731	-	-			
(10 years)	Smoking habit	17 352	13	70	248	_	-			
	Chewing habit	5016	15	250	15 491	60	300			
	Mixed habits	5879	45	600	175	-	-			
	Total	34 039	73	210	40 645	60	130			
Bhavnagar (12)	No habit	11 377	-	-	34 783	-	-			
(10 years)	Smoking habit									
	Bidi	12 352	40	290	51	-	-			
	Clay pipe	3319	29	670	32	-	-			
	Others	1694	10	440	17	1	1130			
	Chewing habit	2877	2	70	123	-	_			
	Mixed habits	1222	4	250	10	-	-			
	Total	32 841	85	240	35 016	1	3			
Srikakulam (12)	No habit	4662	_	_	6920	-	-			
(10 years)	Smoking habit									
(non-palatal	Conventional	8216	17	170	78	_	-			
leukoplakias)	Reverse	7524	11	100	13 752	2	30			
1 /	Chewing habit	910	2	140	664	_	_			
	Mixed habits	1620	2	80	199	_	_			
	Total	22 932	32	110	21 433	2	20			
This study	No habit	96	0	_	66	0		27	0.0%	
(quid lesion)	Ex-chewing habit	126	ŏ	_	144	ŏ	_	46	0.0%	
(6 years)	Chewing habit	253	ĩ	385	479	ž	133	121	2.5%	
(0)0010)	Total	475	1	116	689	2	108	194	1.5%	

incidence (384.6 vs. 132.9 per 100 000 person-years). There was only one woman developed SCC. Hence, it yielded the total incidence rate of 89.6 per 100 000.

Discussion

As our study sample is a relatively small number of participants and weekly visits were provided, the

authors were able to follow-up all of the 194 participants.

The risk for developing oral mucosal lesions from chewing areca/betel quid had been reported in many countries. For the oral condition of OSF, a prevalence rate of 3.03% was identified in the Xiangtan City of China with a 35.37 areca quid chewing prevalence (6). In Pakistan (7), studies have indicated that the odds ratio

Table 6 Comparisons of age-adjusted incidence rates (per 100 000 person-years) of OSF in India with the current study

		Male			Female		Total		
Area (years of follow-up)	Habits	Person- years	New cases	Incidence per 100 000 person- year	Person- years	New cases	Incidence per 100 000 person-year	Number of persons	% of new cases
Gujarat (11)	No habit							7065	0.1%
(2 years in 43 654	Betel quid							2105	0.3%
factory workers)	Betel quid and smoke							9506	0.1%
	Tobacco quid							1161	0.3%
Ernakulam (12)	No habit	5840	-	-	25 122	-	_		
(10 years)	Smoking habit	19 933	-	-	289	-	-		
· · /	Chewing habit	5829	2	35	17 282	8	29		
	Mixed habits	8226	1	7	230	_	-		
	Total	39 828	3	7	42 923	8	17		
Bhavnagar (12) (10 years)	Total	38 818	1	3	35 278	3	9		
This study	No habit	96	0	_	66	0	_	27	0.0%
(6 years)	Ex-chewing habit	126	0	_	144	0	_	46	0.0%
	Chewing habit	253	1	385	479	1	286	121	1.7%
	Total	475	1	161	689	1	213	194	1.0%

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of having OSF for betel quid was 32, and the odds ratio for betel quid with tobacco was 64. Similar risks were also reported for other oral mucosal lesions including: Hainan Island of China (8), Thailand (9), Cambodian (10), and India (11).

The incidence rates of oral pre-cancerous lesions were rarely reported in the past. In this study, the new lesions found from the 1997 survey sample were primarily (four of five) from areca/betel quid chewers without any prior history of using any types of tobacco products. Only one man with both betel quid chewing and cigarette smoking habits developed quid lesion and OSF. As the areca/ betel quid in Taiwan does not contain any tobacco products, it is clear that the areca/betel quid itself can lead to oral pre-cancerous lesions without any effects from tobacco related products. It is also important to note that no new pre-cancerous lesions were identified from those who did not have any areca/betel quid chewing habit in 1997 [30.5% from Yang et al. (2)]. Therefore, simply stopping the chewing habit is the most effective way of oral cancer prevention.

Unlike the incidence rates of oral cancer, which are available for many countries with a cancer registry system, the incidence rates of various oral lesions were only previously reported from India. In terms of quid lesion, two women with biopsy confirmed lesions of hyperparakeratosis and epithelial hyperplasia, and one man with hyperparakeratosis were encountered. For men with chewing habits, our results showed an incidence rate of 385 new lesions per 100 000 personyears with new quid lesion. For women with areca/betel quid chewing habit, one can find 133 new quid lesions in 100 000 person-years. Table 5 has the comparison of the incidence rates of quid lesions with those of leukoplakia from studies in India, for people with habits of betel quid chewing only and mixed habits (betel quid chewing and tobacco) in India. The incidence rate of quid lesion for people with chewing habit of this study was much higher than those of leukoplakia in communities of India (12), and were smaller than those from factory workers (11) and policemen (13) in India. Although the areca/betel quid in Taiwan does not contain tobacco, the incidence rates can still be higher than India's, where the majority of the betel quid contains tobacco.

For the oral pre-cancerous condition, OSF, Gupta's report in 1980 (12) had < 50 per 100 000 person-years for both chewing and mixed habits. Our study showed an incidence rate of 385 for men and 286 for women (Table 6). In the Mutan community, the incidence rates of OSF were much higher than those from India's.

There was only one woman found to have oral cancer in the buccal mucosa. The incidence rate of women was 89.6 per 100 000 person-years. From a brief review of oral cancer (ICD-9 140–141, 143–145) incidence rates of 1994–1996 in the general Taiwanese female population (14), one can obtain the number of 1.63 per 100 000 person-years given than only 1.1% of the female population chewed areca/betel quid (1). The incidence rates computed from Parkin et al. (4) were 10.97, 10.65, 10.2, 7.68 and 7.24, respectively, for Karunagappally, Madras, Bangalore, Trivandrum and Mumbai. Altho-

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ugh only one case cannot account for a legitimate oral cancer incidence rate, the rate found in this study indicated a serious problem in the Mutan community.

Despite all computed incidence rates have shown important message for areca/betel quid chewing habits, the fact that small follow-up number of persons is the major limitation for this research. Large-scale of followup studies will still need to be undertaken for a statistical significant result.

Our study not only obtained the incidence rates for oral pre-cancerous lesions from a different population other than India, but was also first to report the incidence rates from a group of people with only areca/betel quid chewing habit and without any prior history of tobacco usage. Nevertheless, it occurred to the authors that without any effects from tobacco products the habit of chewing areca/betel itself is definitely related to oral pre-cancerous lesions and oral cancer.

The total number of persons followed in this study was relatively small, and hence, it led to only single digit of new cases for different lesions as well as large ranges of confidence intervals. Therefore, no significant incidence rates were obtained from this follow-up study.

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